REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1, 3, 5, 7-9, 11-12, 14-21 and 23-26 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Claim dependencies are corrected.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case of obviousness requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. An inquiry is required as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." Id. at 1396. But a claim directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id.

Claims 1-3, 6-9, 11-12 and 19-21 were rejected under Section 103 as allegedly unpatentable over Ji (EP 1172373, the family name of the inventor is not Sung) in view of Dekker et al. (US 2004/0241664) and van Loon et al. (US 6,713,082). Applicants traverse.

Ji relates to use of a zinc oligopeptide of six amino acids and having a molecular weight of 800 to 1200 daltons (see paragraph [0023]). But it does not disclose any di- or tripeptides. Zinc is involved in the onset of diabetes mellitus; it is described to have a physiological activity associated with sugar control and vigor in the body (see paragraph [0003]). The oligopeptide is absorbed by the body (see paragraphs [0012] and [0016]). Thus, the combination of zinc and oligopeptide is intended to increase absorption of Ji's composition by the human body. The function of the peptide is nothing else than to enhance absorption of zinc by the body. Ji does not disclose any other use for the oligopeptide. Therefore, the primary document relates only to the use of an oligopeptide to increase the absorption of the zinc by the human body. Since there is no evidence of record that di- or tripeptides (and optionally free amino acids) would have the same biological activity as Ji's oligopeptide to enhance absorption of zinc by the body, their inclusion in Ji's composition would not have been obvious to one of ordinary skill in the art. Why would one of ordinary skill in the art have included them otherwise?

By contrast, Applicants' claimed composition requires "at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da." The Examiner admits that Ji does not teach that "at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da" (page 6 of the Office Action). It is the presence of a significant proportion of such small peptides (and optionally free amino acids) that is responsible for the efficacy of the claimed composition. Potentiation of the insulin sensitizer's activity by small peptides (e.g., di- and/or tripeptides) was not taught or rendered obvious by the prior art. A determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976). Here, no evidence was provided in the Office Action to show a reasonable expectation of success of using small peptides (and the optionally free amino acids) to potentiate the activity of insulin sensitizers. Therefore, Applicants' claimed invention is patentable because a prima facie case of obviousness was not established.

Dekker mentions a peptide fraction. But it does not disclose a peptide fraction containing a high proportion of di- and/or tripeptides; nor does it teach or suggest combining the peptide fraction with an insulin sensitizer. The Examiner's allegation that

"protein hydrolysate fractions with variable molar %'s (including 61%, nearly the at least 70 molar % Applicant has amended to) and peptides with a molecular weight below 2000 Da" (page 6 of the Office Action) is incorrect. Cf. "peptides that carry a carboxy terminal proline residue represent a molar fraction of 61% of the total of the peptides present in the molecular weight range between 400 and 2000 daltons" in Dekker's paragraph [0216]. Dekker does not disclose how much of the peptide fraction are peptides having molecular weights below 2000 daltons. Of course, a large number of the peptides in the hydrolysate have a carboxy terminal proline. But this emphasis on peptides containing carboxy-terminal proline teaches away from combining Ji and Dekker because Ji's oligopeptide contains no proline anywhere in its sequence (see formula I). Why would one of ordinary skill in the art combine the compositions of Ji and Dekker? There is also no evidence of record that Dekker's peptides would enhance absorption of zinc by the body, and adding Ji's oligopeptide would only reduce the molar fraction of the peptides in the composition having a carboxy terminal proline.

van Loon relates to hydrolysates combined with the two free amino acids leucine and phenylalanine to enhance the blood insulin level in a healthy person after physical exercise (see abstract and claim 24). Col. 1, lines 38-50, explains that this composition consisting of hydrolysate and two specified free amino acids is used to stimulate the plasma insulin response, the synthesis of muscle glycogen, and recovery when taken after exercise. van Loon has nothing to do with diabetic patients, nor does the cited document teach or render obvious an insulin sensitizer in combination with small peptides (e.g., di- and/or tripeptides). The specific proportions of small peptides required by Applicants' claimed composition are neither taught nor rendered obvious. In the three examples, van Loon tests a group of healthy male subjects (study 1), male athletes (study 2), and male athletes (study 3). Thus, all of the subjects were persons who would not be treated with an insulin sensitizer for diabetes. Why would one of ordinary skill in the art combine the compositions of Ji and van Loon? There is no evidence of record that van Loon's free amino acids would enhance absorption of zinc by the body, and no reason was provided for combining Ji's treatment of diabetes with free amino acids as the latter would not have been expected to have any beneficial effect on patients.

Contrary to the Examiner's allegation on page 7 of the Office Action that it would be routine to optimize the molar% of peptides having a molecular weight below 2000 Da, no evidence of record was cited or acceptable reason was provided in the Office Action that one of ordinary skill in the art would find such optimization routine. Why would one of ordinary skill in the art include at least 70 molar% of such small peptides when no reason is provided that high proportions of small peptides would have a beneficial effect nutritionally or therapeutically?

Prima facie obviousness requires there have been a reasonable expectation of success. See *Rinehart*. No evidence of a reasonable expectation of success to enhance the blood insulin response by combining the compositions of Ji, Dekker and van Loon was cited on page 7 of the Office Action. Instead, the Examiner merely asserts that the "teachings of the references" show there would have been a reasonable expectation of success. This is not acceptable basis for a Section 103 rejection. Therefore, Applicants submit that a prima facie case of obviousness was not established because evidence was not cited in the Office Action. If this rejection is maintained, it is respectfully recited that specific portions of the cited documents be cited in the next nonfinal Office Action so Applicants can have an adequate opportunity to respond.

Applicants' claimed invention requires "at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da" (see claim 1). Where in the cited documents is this limitation disclosed or rendered obvious?

Moreover, Applicants' claimed invention requires "at least 20 molar% of peptides with a molecular weight below 2000 Da are present as di- and/or tripeptides" (see claim 1). Where in the cited documents is this limitation disclosed or rendered obvious?

The limitations of Applicants' dependent claims were also disregarded in the Office Action. Claim 7 requires that "most of the di- and/or tripeptides are comprised of proline at one end." Claim 8 requires that "at least 20% of proline present in the hydrolyzed protein is present in the di- and/or tripeptides." Claim 9 requires that "at least 30% of the tripeptides have a carboxy terminal proline." Where in the cited documents are these limitations disclosed or rendered obvious? It is improper for limitations of claims 7-9 to be disregarded when comparing Applicants' invention to the prior art. It needs to be

made of record in an obviousness rejection whether the claim limitations are disclosed in the cited documents because such is a prerequisite for determining the differences between the claimed invention and the prior art. See the *Graham* factors. And in the absence of evidence to the contrary in the Office Action (such evidence being absent because the Examiner deemed it immaterial to perform the *Graham* analysis), it must be concluded as a matter of law from the failure by the Patent Office to carry its burden of going forward with acceptable evidence that a prima facie case of obviousness has not been established. The Examiner is urged to complete the record by complying with the requirements of *Graham* and citing where each claim limitation is found in the prior art (and explicitly admitting when claim limitations are neither taught nor rendered obvious by the prior art). Modifications to the rejection of record by new citations to the documents of record should be made in a nonfinal Office Action to give Applicants an adequate opportunity to respond.

Withdrawal of the Section 103 rejection is requested because the claims would not have been obvious to one of ordinarily skill in the art when this invention was made.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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